

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EPO

# PCT

## CHAPTER II

### DEMAND

under Article 31 of the Patent Cooperation Treaty:  
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA		Date of receipt of DEMAND	
<b>Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION</b>		Applicant's or agent's file reference <b>P019602W0</b>	
International application No. <b>PCT/GB99/02391</b>	International filing date (day/month/year) <b>22/07/1999</b>	(Earliest) Priority date (day/month/year) <b>24/07/1998</b>	
Title of invention <b>ANTI-INFLAMMATORY COMPOUNDS</b>			
<b>Box No. II APPLICANT(S)</b>			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  <b>WILLIAM HARVEY RESEARCH LIMITED</b> <b>Charterhouse Square</b> <b>London</b> <b>EC1M 6BQ</b> <b>United Kingdom</b>		Telephone No.:	
		Facsimile No.:	
		Teleprinter No.:	
State (that is, country) of nationality: <b>UNITED KINGDOM</b>		State (that is, country) of residence: <b>UNITED KINGDOM</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  <b>PERRETTI, Mauro</b> <b>Flat 1</b> <b>203 Goldhurst Terrace</b> <b>London</b> <b>NW6 3ER</b> <b>UNITED KINGDOM</b>			
State (that is, country) of nationality: <b>ITALY</b>		State (that is, country) of residence: <b>UNITED KINGDOM</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  <b>FLOWER, Roderick</b> <b>7 Tithe Barn Court</b> <b>Dairy Way</b> <b>Abbots Langley</b> <b>Hertfordshire</b> <b>WD5 OTB</b> <b>United Kingdom</b>			
State (that is, country) of nationality: <b>UNITED KINGDOM</b>		State (that is, country) of residence: <b>UNITED KINGDOM</b>	
<input type="checkbox"/> Further applicants are indicated on a continuation sheet.			

**Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**The following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*HOWARD, Paul Nicholas  
CARPMAELS & RANSFORD  
43 BLOOMSBURY SQUARE  
LONDON WC1A 2RA  
UNITED KINGDOM

Telephone No.:

020-7242 8692

Facsimile No.:

020-7405 4166

Teleprinter No.:

267209

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments:\***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filedthe description ☐ as originally filed☐ as amended under Article 34the claims ☐ as originally filed☐ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34the drawings ☐ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

\* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

**Box No. VI CHECK LIST**

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- |  |   |        |
|--|---|--------|
| 1. translation of international application                              | : | sheets |
| 2. amendments under Article 34   | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19  | : | sheets |
| 5. letter  | : | sheets |
| 6. other ( <i>specify</i> )  | : | sheets |

For International Preliminary  
Examining Authority use only

received                      not received

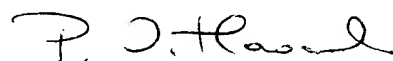
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- |  |   |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet                             | 4. <input type="checkbox"/> statement explaining lack of signature                                  |
| 2. <input type="checkbox"/> separate signed power of attorney                            | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney, reference number, if any: | 6. <input type="checkbox"/> other ( <i>specify</i> ):   |

**Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE**

*Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).*



HOWARD, Paul Nicholas (Authorised Agent)

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>P0196002W0</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 99/02391</b>	International filing date (day/month/year) <b>22/07/1999</b>	(Earliest) Priority Date (day/month/year) <b>24/07/1998</b>
Applicant  <b>WILLIAM HARVEY RESEARCH LIMITED et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/02391

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 7-8 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	LIM L H ET AL.: "PROMOTING DETACHMENT OF NEUTROPHILS ADHERENT TO MURINE POSTCAPILLARY VENULES TO CONTROL INFLAMMATION EFFECT OF LIPOCORTIN 1" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA (1998 NOV 24) 95 (24) 14535-9, XP002130358 the whole document	1-8
X	CROXTALL J D ET AL.: "N-TERMINAL PEPTIDE FRAGMENTS OF LIPOCORTIN-1 INHIBIT A549 CELL GROWTH AND BLOCK EGF-INDUCED STIMULATION OF PROLIFERATION" INTERNATIONAL JOURNAL OF CANCER (1993 APR 22) 54 (1) 153-8, XP000876677 abstract page 155, column 1, paragraph 1	1,2,8

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## ° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

14 February 2000

Date of mailing of the international search report

28/02/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Cervigni, S

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PERRETTI M ET AL.: "LIPOCORTIN-1 FRAGMENTS INHIBIT NEUTROPHIL ACCUMULATION AND NEUTROPHIL-DEPENDENT EDEMA IN THE MOUSE A QUALITATIVE COMPARISON WITH AN ANTI-CD11B MONOCLONAL ANTIBODY" JOURNAL OF IMMUNOLOGY (1993 OCT 15) 151 (8) 4306-14, XP002130360 abstract	
A	US 4 950 646 A (WALLNER BARBARA P ET AL) 21 August 1990 (1990-08-21)	

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/02391

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4950646 A	21-08-1990	US 4879224 A	07-11-1989
		AT 108830 T	15-08-1994
		AU 601676 B	20-09-1990
		AU 5318286 A	29-07-1986
		DE 3689977 D	25-08-1994
		DE 3689977 T	27-10-1994
		DK 433686 A	10-09-1986
		EP 0209568 A	28-01-1987
		ES 550784 A	16-03-1987
		FI 863626 A	09-09-1986
		HU 40695 A	28-01-1987
		JP 7089996 A	04-04-1995
		JP 7087980 A	04-04-1995
		JP 7101994 A	18-04-1995
		JP 7087789 B	27-09-1995
		JP 62501679 T	09-07-1987
		WO 8604094 A	17-07-1986
		US 5081019 A	14-01-1992
		US 4874743 A	17-10-1989
		ZA 8600217 A	27-08-1986

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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>P019602WO</b>	<div style="display: flex; justify-content: space-between;"> <div><b>FOR FURTHER ACTION</b></div> <div>See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)</div> </div>	
International application No. <b>PCT/GB99/02391</b>	International filing date ( <i>day/month/year</i> ) <b>22/07/1999</b>	Priority date ( <i>day/month/year</i> ) <b>24/07/1998</b>
International Patent Classification (IPC) or national classification and IPC <b>C07K14/47</b>		
Applicant <b>WILLIAM HARVEY RESEARCH LIMITED et al.</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  <b>20/01/2000</b>	Date of completion of this report  <b>3. 10. 00</b>
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  <b>Pilat, D</b>  Telephone No. +49 89 2399 8668  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/02391

**I. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

**Description, pages:**

1-10 as originally filed

**Claims, No.:**

1-8 as received on 22/09/2000 with letter of 20/09/2000

**Drawings, sheets:**

1/2,2/2 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**II. Priority**

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- ☐ copy of the earlier application whose priority has been claimed.
- ☐ translation of the earlier application whose priority has been claimed.
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/02391

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**see separate sheet**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 7,8.

because:

- ☒ the said international application, or the said claims Nos. 7,8 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/02391

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	1-8
	No:	Claims	
Inventive step (IS)	Yes:	Claims	4
	No:	Claims	1-3,5-8
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

**2. Citations and explanations**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

***Ad Section I: Basis of the report***

1. Reference is made to the following documents:

D1: CROXTALL J D ET AL.: 'N-TERMINAL PEPTIDE FRAGMENTS OF LIPOCORTIN-1 INHIBIT A549 CELL GROWTH AND BLOCK EGF-INDUCED STIMULATION OF PROLIFERATION' INTERNATIONAL JOURNAL OF CANCER (1993 APR 22) 54 (1) 153-8, XP000876677

- 1.1 The documents D2 and D3 were not cited in the international search report. Copies of the documents are appended hereto.

D2 I. T. PAULSEN ET AL.: "Characterization of sin, a potential recombinase-encoding gene from Staphylococcus aureus" . Gene (141 (1994) p.109-114  
D3 P. DEZELEE ET AL.: " Small Deletion in v-src SH3 Domain of a Transformation Defective Mutant of Rous Sarcoma Virus Restores Wild Type Transforming Properties". Virology (189 (1992) p.556-567).  
D4 J.D. Croxtall et al.: "Inhibitory effect of peptides derived from the N-terminus of lipocortin 1 on arachidonic acid release and proliferation in the A549 cell line: identification of E-Q-E-Y-V as a crucial component". British Journal of Pharmacology (1998) 123, p-975-83.

**2) Amendments (Article 34(2)(b) PCT)**

The amendments introduced by the applicant appear to be supported by the present description.

Amended claim 1 is supported by the teaching of the application as a whole, but more particularly by original claim 5.

Amended claim 2 is inter alia based on teaching provided at p.3 lines 22-25 of the present description.

***Ad Section II :Priority***

**3 Priority (Article 8 PCT)**

The document indicated in the search report as a P-document is not to be regarded as state of the art according to Article 33 (2) PCT, as the date of priority claimed can be allowed for claims 1 to 8 of the present application.

***Ad Section III :Non-establishment of opinion***

Claims 7,8 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT) (see also point 6 below).

***Ad Section V :Reasoned statement under Rule 66.2(a)(ii); citations and explanations supporting such statement***

**4. Novelty (Article 33 (2) PCT)**

- 4.1 None of the document cited in the international search report discloses a compound as claimed in claim 1 for therapeutic use. Thus, claim 1 seems novel. The same conclusion applies to dependent claims 2-4 and to claims 5-8 referring directly or indirectly to claim 1.
- D1 describes an amino terminal peptide fragment of lipocortin-1 starting at position 1 and ending at position 12 (see abstract). It was not used in therapy. D2 and D3 refer to a RSV src gene product and to a Staphylococcus aureus sin gene product, a potential recombinase, respectively. They do not disclose a use in therapy either.

**5. Inventive step (Article 33 (3) PCT)**

- 5.1 Claim 1 covers both the PA101T src gene product (see D3) and the potential recombinase-encoding sin gene product (see D2). The present application relates to the N-terminal fragments of LC-1 which were found to have in-vivo anti-inflammatory properties.
- However, the product of D2 and D3 will almost certainly not have in-vivo anti-inflammatory properties as identified for N-terminal LC-1 fragments in the present description.

As a consequence, since claim 1 includes products which will almost certainly not solve the problem posed, said claim is not adequately supported over its entire breadth (see also PCT Guidelines 6.1-6.3). Therefore, if the subject-matter of claim 1 does not solve a particular problem, no inventive step can be acknowledged for said subject-matter. The use in therapy does not modify this conclusion. The same rationale applies to claims 2, 3 and for claims 5-8 referring thereto (see also point 7 below).

- 5.2 D1 is considered to represent the most relevant state of the art. It discloses amino terminal peptide fragments of lipocortin-1 (see point 4.1 above) and states that peptide 1-12 is inactive (see abstract). It describes that this peptide has no significant effect on A549 cell growth at any concentration and at any time in culture (see left column result section 1.st paragraph; Figs 1 and 2). However, said peptide which has no growth inhibitory properties by itself can reverse EGF-induced stimulation of proliferation of these cells (see p.155 left column 1.st paragraph; Figs 1 and 5). Thus, peptide 1-12 does not significantly affect PGE<sub>2</sub> release but blocks the EGF-induced increase in PGE<sub>2</sub> release (see p.155 left column).

The difference between D1 and the subject-matter of claim 4 is that it provides a peptide which is AMVSEFLKQAW.

The problem to be solved by the present invention may therefore be regarded as to obtain a compound with in vivo anti-inflammatory properties.

Faced with this problem, the skilled person would have repeated the experiments recited in D1. Apparently, in doing so, he would have failed to inhibit the activation of cPLA<sub>2</sub> with LC-1 peptide 1-12, when A549 cells were treated with EGF, and consequently would have failed to block the cPLA<sub>2</sub>-mediated release of eicosanoids, which includes PGE<sub>2</sub>. These results are contrary to the findings in D1 (see also expert opinion D4 p.976, first column "Use of EGF", p.980 first column "effect of peptides on cPLA<sub>2</sub> activity").

Since the results reported in D1 seems erroneous with regard to peptide 1-12 and there is no indication in D1 that would prompt the skilled person to select peptide 1-12 or AMVSEFLKQAW to solve the problem posed, the skilled person would not have arrived at the subject-matter of claim 4 without inventive activity. Thus, the solution proposed in claim 4 appears to involve an inventive step.

**6) Industrial applicability (Article 33 (4) PCT)**

For the assessment of the present claims 7,8 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment or in diagnostic methods, but may allow, however, claims to a known compound for first use in medical treatment or diagnostic method and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Ad Section VIII : Certain observations on the international application.**

**7) Clarity (Article 6 PCT)**

The applicant is reminded that claim 1 encompasses at present all the compounds comprising at least AMVSE but not EQEYVQTV, whatever function these compounds may have. Due to this broad formulation, it embraces unrelated prior art compounds which do not solve the problem underlying the present application (see also D2 and D3). As a consequence, claim 1 lacks essential features and accordingly lacks clarity (see also point 5.1 above)



Claims

1. A compound comprising the amino acid sequence AMVSE, wherein said compound does not comprise the amino acid sequence EQEYVQTV, for use in therapy.  
5
2. A compound according to claim 1 for inhibiting leukocyte migration, or treating or preventing inflammation and/or inflammatory response/disease.
3. A compound according to claim 1 or 2 which is a polypeptide.  
10
4. A compound according to any one of claims 1 to 3 which is AMVSEFLKQAW.
5. A pharmaceutical composition which comprises a compound according to any preceding claim and which further comprises one or more pharmaceutically acceptable  
15 excipients.
6. Use of a compound according to any one of claims 1 to 4 or a composition according to claim 5 in the manufacture of a medicament for inhibiting leukocyte migration, or treating or preventing inflammation and/or inflammatory  
20 response/disease.
7. A method of inhibiting leukocyte migration, or treating or preventing inflammation and/or inflammatory response/disease, comprising administering to an animal an effective amount of a compound according to any one of claims 1 to 4 or a  
25 composition according to claim 5.
8. Use according to claim 6 or a method according to claim 7, wherein the inflammatory response/disease is gout, gouty arthritis, rheumatoid arthritis, asthma, reperfusion injury or damage, stroke, myocardial infarction, septic shock, or a skin  
30 disorder.

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International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>C07K 14/47, A61K 38/17</b>	<b>A2</b>	<b>(11) International Publication Number:</b> <b>WO 00/05255</b>
		<b>(43) International Publication Date:</b> 3 February 2000 (03.02.00)
<b>(21) International Application Number:</b> PCT/GB99/02391 <b>(22) International Filing Date:</b> 22 July 1999 (22.07.99) <b>(30) Priority Data:</b> 9816235.7 24 July 1998 (24.07.98) GB <b>(71) Applicant (for all designated States except US):</b> WILLIAM HARVEY RESEARCH LIMITED [GB/GB]; Charterhouse Square, London EC1M 6BQ (GB). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> PERRETTI, Mauro [IT/GB]; Flat 1, 203 Goldhurst Terrace, London NW6 3ER (GB). FLOWER, Roderick [GB/GB]; 7 Tithe Barn Court, Dairy Way, Abbots Langley, Hertfordshire WD5 0TB (GB). <b>(74) Agents:</b> HOWARD, Paul, Nicholas et al.; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>
<b>(54) Title:</b> ANTI-INFLAMMATORY COMPOUNDS		
<b>(57) Abstract</b> <p>A compound comprising the amino acid sequence AMVSE, wherein said compound does not comprise the amino acid sequence EQEYVQTV. The compound is useful as an anti-inflammatory agent.</p>		